

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Present Application:**

Applicant : Emad. S. Alnemri  
Title : TRAIL RECEPTORS, NUCLEIC ACIDS ENCODING THE SAME,  
AND METHODS OF USE THEREOF (AS AMENDED)  
Docket No. : 480140.432D3  
Date : February 12, 2002

**Prior Application:**

Examiner : Prema Mertz, Ph.D.  
Art Unit : 1646  
Application No. : 09/134,618

Box Patent Application  
Commissioner for Patents  
P.O. Box 2327  
Arlington, VA 22202

**PRELIMINARY AMENDMENT**

Commissioner for Patents:

Please amend the above-identified application as follows:

**In the Specification:**

On page 1, please amend the title of the application to read:

TRAIL RECEPTORS, NUCLEIC ACIDS ENCODING THE SAME, AND  
METHODS OF USE THEREOF

On page 1, line 4, please replace the section entitled "CROSS-REFERENCE TO RELATED APPLICATION" with the following:

This application is a divisional based off of U.S. Application No. 09/134,618, filed August 14, 1998; which application claims priority from United States Provisional Application No. 60/055,906, filed August 15, 1997, now abandoned; which applications are herewith incorporated herein in their entirety.

In the Claims:

Please cancel claims 1-27.

Please amend claim 28 to read:

28. (Amended) A bioassay for evaluating whether test compounds are capable of acting as agonists or antagonists for DR5 or TRAIL-R3 proteins wherein said protein is characterized by being able to bind TRAIL ligand, said bioassay comprising:

(a) culturing cells containing: DNA which expresses DR5 or TRAIL-R3 proteins or functional modified forms thereof, wherein said culturing is carried out in the presence of at least one compound whose ability to modulate apoptotic activity of DR5 or TRAIL-R3 protein is sought to be determined, and thereafter

(b) monitoring said cells for either an increase or decrease in the level of apoptosis.

Please amend claim 29 to read:

29. (Amended) A bioassay for evaluating whether test compounds are capable of acting as antagonists for DR5 or TRAIL-R3 proteins wherein said protein is encoded by a nucleotide sequence that is substantially the same as SEQ ID NO:1, SEQ ID NO:3, or SEQ ID

NO:5 or functional modified forms of said DR5 or TRAIL-R3 proteins, said bioassay comprising:

(a) culturing cells containing: DNA which expresses DR5 or TRAIL-R3 proteins, or functional modified forms thereof, wherein said culturing is carried out in the presence of: increasing concentrations of at least one compound whose ability to inhibit apoptotic activity of DR5 or TRAIL-R3 proteins is sought to be determined, and a fixed concentration of TRAIL; and thereafter

(b) monitoring in said cells the level of apoptosis as a function of the concentration of said compound, thereby indicating the ability of said compound to inhibit DR5 or TRAIL-R3 apoptotic activity.

#### REMARKS

Claims 28-30 are pending in the instant application. Claims 1-27 have been cancelled without prejudice to the filing of additional continuation, continuation-in-part or divisional applications. Claims 28 and 29 have been amended to more clearly define the invention. The title to the instant application has been amended to remove the word "Novel". The cross reference section to the application has been updated. Although this section of the application is no longer required, Applicant has included this section in order to more clearly indicate which applications may be incorporated by reference. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

All of the claims remaining in the application are now clearly allowable.  
Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Seed Intellectual Property Law Group PLLC



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the above-identified application as follows:

In the Specification:

On page 1, please amend the title of the application as follows:

~~NOVEL~~ TRAIL RECEPTORS, NUCLEIC ACIDS ENCODING THE SAME,  
AND METHODS OF USE THEREOF

On page 1, line 4, please replace the section entitled "CROSS-REFERENCE TO  
RELATED APPLICATION" with the following:

This application is a divisional based off of U.S. Application No. 09/134,618,  
filed August 14, 1998; which application claims priority from United States Provisional  
Application No. 60/055,906, filed August 15, 1997, now abandoned; which applications are  
herewith incorporated herein in their entirety.

In the Claims:

Claims 1-27 have been cancelled.

Claim 28 has been amended as follows:

28. (Amended) A bioassay for evaluating whether test compounds are capable  
of acting as agonists or antagonists for DR5 or TRAIL-R3 proteins wherein said protein is  
characterized by being able to bind TRAIL ligand according to claim 15, said bioassay  
comprising:

(a) culturing cells containing: DNA which expresses DR5 or TRAIL-R3 proteins or functional modified forms thereof, wherein said culturing is carried out in the presence of at least one compound whose ability to modulate apoptotic activity of DR5 or TRAIL-R3 protein is sought to be determined, and thereafter

(b) monitoring said cells for either an increase or decrease in the level of apoptosis.

Claim 29 has been amended as follows:

29. (Amended) A bioassay for evaluating whether test compounds are capable of acting as antagonists for DR5 or TRAIL-R3 proteins ~~according to claim 18~~, wherein said protein is encoded by a nucleotide sequence that is substantially the same as SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5 or functional modified forms of said DR5 or TRAIL-R3 proteins, said bioassay comprising:

(a) culturing cells containing: DNA which expresses DR5 or TRAIL-R3 proteins, or functional modified forms thereof, wherein said culturing is carried out in the presence of: increasing concentrations of at least one compound whose ability to inhibit apoptotic activity of DR5 or TRAIL-R3 proteins is sought to be determined, and a fixed concentration of TRAIL; and thereafter

(b) monitoring in said cells the level of apoptosis as a function of the concentration of said compound, thereby indicating the ability of said compound to inhibit DR5 or TRAIL-R3 apoptotic activity.